Gender Differences in Therapy for Patients Admitted for Unstable Angina and Myocardial Infarction with Underlying Chronic Kidney Disease

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Abstract

We examined treatment patterns of female pts with CKD admitted for ACS. In this retrospective review of 200 patients with chronic kidney disease presenting with acute coronary syndrome, we found that females patients were less likely to receive aspirin and ACE-inhibitors and there was a trend towards less frequent use of coronary angiography.

Introduction

Coronary heart disease (CHD) continues to be the leading cause of morbidity and mortality among persons in industrialized countries. In addition, patients with chronic kidney disease (CKD) have a high prevalence of cardiovascular disease and cardiac death. In the United States, cardiac disease accounts for 44% of overall mortality in chronic dialysis patients.[1] Recent data support the application of proven interventions in the general population, such as angiotensin-converting enzyme inhibitors and statins to patients with CKD and ESRD.[2,3] Each year more than 1 million American women and men are diagnosed with acute myocardial infarction (AMI) Previous studies looking at sex differences in management of acute coronary syndromes (ACS) found that women were less likely to undergo more invasive treatments than men.[4,5,6] Other studies also report that women are less likely to undergo both diagnostic and revascularization procedures than men.[7,8,9]

There is a lack of data evaluating gender differences in the management of ACS in patients with CKD. The purpose of this study is to evaluate gender differences in treatment patterns of patients with CKD presenting with ACS.

Methods

Demographic and clinical data were extracted as specified in the results section. Bleeding was defined as either minor or major bleeding episode following the TIMI-bleeding criteria (reference). We categorized participants into two groups based on the existence of chronic renal failure. Normally distributed data is reported as mean and standard deviation (SD), non-normally data is presented as median and interquartile range. Characteristics between the two groups were compared by Chi-Square for dichotomous variables and Mann-Whitney U Test and Student's T-test for continuous variables. To determine the independent association between incidence of bleeding and other cofactors including CKD we used binary logistic regression analysis to calculate odds ratios. The study was a retrospective analysis of patients with CKD who presented to two major hospitals in the metropolitan area of Honolulu, Hawaii from January 2001 to June 2003. Patients carrying an ICD 9 code for ACS and CKD as a primary or secondary diagnosis were included.

Patients with a Creatinine less than 1.5 were excluded from the study. Criteria for diagnosis of ST-segment elevation AMI includes ischemic-type chest discomfort of >30 minutes with electrocardiogram evidence of ST-segment elevation ≥0.2 mV in ≥2 contiguous precordial leads of ST-segment elevation ≥0.1 mV in ≥2 limb leads and an elevated serum creatine kinase-MB level (>10%) or an elevated serum cardiac-specific troponin I level (>2 ng/ml). Non-ST-segment elevation AMI was diagnosed by ischemic-type chest discomfort of >30 minutes without ST-segment elevation but with an elevated serum creatine kinase-MB or a cardiac-specific troponin I level.[10] Unstable angina was diagnosed by ischemic-type chest discomfort of >30 minutes with normal serum creatine kinase-MB and cardiac-specific troponin I levels. Data on demographics, cardiac risk factors, presenting symptoms, diagnostic tests and therapeutic interventions were gathered from the patient's medical records. Killip classification was defined using the collected data in order to assess symptoms of heart failure. Statistical analyses was done using chi-square, Student's t-test and Mann-Whitney U test to determine differences in management between the two treatment groups.

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Table 1.— Baseline Characteristics for Women and Men			
Variable	Women (n=97)	Men (n=104)	*P* value
Age (years) [mean ± SD]	68 ± 13.8	70 ± 2.8	NS
Comorbidities (%)			
Previous myocardial infarction	42.3	39.4	NS
Previous PCI	15.5	9.6	NS
Previous CABG	26.8	27.9	NS
Hypertension	89.7	86.5	NS
Diabetes	67.0	43.3	NS
Hyperlipidemia	43.3	36.5	NS
Obesity*	7.2	7.7	NS
Smoking	5.2	10.6	NS
Family history of CAD	25.8	14.4	0.044
Troponin I max (ng/mL)			
Median [interquartile range]	2.3 [0.26-19.77]	2.7 [0.27-16.75]	NS
Creatinine kinase-MB max (U/L)			
Median [interquartile range]	8.4 [3.6-18.8]	8.3 [4.7-20.8]	NS
LV ejection fraction			
Mean ± SD	45% ± 16.6	42% ± 14.3	NS
Killip class (%)			
I	36.1	50	0.03
II	38.1	33.7	NS
III	25.8	14.4	0.044
IV	0	2.3	NS

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; PCI, percutaneous coronary intervention; LV, left ventricular
*Obesity defined as BMI≥25.

Results

The study included 97 women, mean age 68 ± 14 years (range 35 to 98), and 104 men, mean age 70 ± 13 years (range 29 to 100) (p=NS). Table 1 shows the prevalence of coronary risk factors in women versus men. Family history of coronary artery disease was statistically more prevalent in women (25.8%) than men (14.4%) (p=0.44). There was no statistically significant difference in severity of disease between women and men. Both groups presented with similar maximum serum creatine kinase-MB and cardiac specific troponin I. In addition, both men and women had similar left ventricular ejection fractions. However, women tended to present with worse Killip classification than men. (Table 1)

There were no significant differences in the rates of non-invasive testing. Both women and men had similar rates of lipid panel evaluation and stress testing (Table 2). Despite these differences in stress testing rates, women were less likely to undergo coronary angiography. Aspirin and ACE-inhibitors were used significantly less frequently in women compared to men. In contrast to these findings, more women were treated with ARBs. (Table 2) The rates of PCI and CABG were similar across both gender groups.

Discussion

Previous studies that assessed gender differences in ACS within the normal population found that women were older than men and had more risk factors and more comorbid conditions.[4,11,12,13] Our study found no age differences between women and men with CKD presenting with ACS, nor were there more risk factors or comorbidities. Despite women presenting with worse symptoms of heart failure, this study found that women with CKD presenting with ACS were less likely to receive aspirin and ACE inhibitors compared to men. Our findings are consistent

Table 2.— Diagnosis and Treatment of Acute Coronary Syndrome in Chronic Renal Failure			
Variable	Women (n=97)	Men (n=104)	*P* value
Non-invasive testing(%)			
Lipids	75.2	76.9	NS
Stress test	32.2	29.4	NS
Invasive testing (%)			
Angiography	26.8	39.4	0.058
Medication (%)			
ACE inhibitor	37	53	0.025
ARB	37	20	0.008
Aspirin	69	83	0.041
Beta-blocker	71	72	NS
Clopidogrel	36	34	NS
Enoxaparin	24	32	NS
GPIIbIIIa	8.3	6.7	NS
IV Heparin	20.6	15.3	NS
Nitropaste	51	48	NS
Statin	52	58	NS
Reperfusion therapy			
PCI	14.4	11.5	NS
CABG	6.2	9.6	NS

Abbreviations: ACE, angiotensinogen converting enzyme; ARB, angiotensin receptor blocker; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

with previous studies looking at gender differences in patients presenting with ACS. These studies found that women were less likely to be treated with aspirin, heparin, or beta-blockers.[14] In contrast to our study, these previous studies did not look specifically at patients with CKD. Based on our results we are unable to explain why there is a difference between the treatment of men and women presenting with ACS. Possible explanations include a lack of knowledge of how prevalent heart disease is in women and a lack of emphasis of treating heart disease in women as compared to men. Further larger studies are needed to determine how significant a difference there is between genders and why this occurs. Of particular interest would be what impact this decreased use of therapy for ACS has on outcomes among the female population presenting with ACS.

In addition to differences in medical therapy between men and women, our study found a decreased utilization of coronary angiography in the female population. These findings are similar to previous research that found that women in all age groups were less likely to undergo diagnostic catheterization than men.[15] In addition, previous studies have found that women were less likely to undergo more aggressive diagnostic evaluation and treatment than men.[16] Reasons for treatment differences between men and women may include a bias towards more conservative therapy in the female population or an under estimation of how large an impact heart disease has on this gender group. Further larger studies are needed to determine how significant a difference there is between genders and why this occurs.

Harrold et al. examined gender differences and trends over time in the management of patients with AMI.[4] These investigators noted that overall, women were less likely to undergo cardiac PCI and CABG. In this study, however, there was no significant difference between revascularization rates among both groups. Possible reason for the difference in our findings compared to other studies may be the overall low incidence of CKD patients undergoing revascularization secondary to comorbidities.

In general this study found that patients with CKD are less likely to undergo revascularization compared to patients without renal insufficiency. This is consistent with previous studies which found that patients with CKD presenting with ACS receive less aggressive treatment.[16,17,18] Perhaps patients with CKD may have more contraindications to aspirin, beta-blockers, and ACE inhibitors. In addition, patients with CKD may have poorer outcome after interventional therapy.

There were several limitations inherent in this study. This study was a small, retrospective, observational, chart review study done at 2 metropolitan Honolulu hospitals, and therefore may not be representative of other hospitals nationwide. In addition, as a retrospective study there is the potential for referral bias.

Conclusions

The results of this study demonstrated that although women with CKD had similar baseline characteristics compared to men with CKD at time of presentation for ACS, women were treated less aggressively. Women were less likely to receive aspirin and were evaluated with cardiac catherization less often than men.

References

1. United States Renal Data System. USRDS 2000 Annual Data Report. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2000; 583-689
2. Mann JF, Gerstien HC, Pogue J, et al. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med 2001;134:629-636
3. Logar CM, Herzog CA, Beddhu S. Diagnosis and therapy of coronary artery disease in renal failure, end-stage renal disease, and renal transplant populations. Am J Med Sci 2003;325:214-227
4. Harrold LR, Esteban J, Lessard D, et al. Narrowing gender differences in procedure use for acute myocardial infarction: insights from the Worcester Heart Attack Study. J Gen Intern Med 2003;18:423-431
5. Chiriboga DE, Yarzebski J, Goldberg RJ, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardio 1993;71:268-273
6. Kostis JB, Wilson AC, O'Dowd K, et al. for the MIDAS Study Group. Sex differences in the management and long term outcome of acute myocardial infarction: a statewide study. Circulation 1994;90:1715-1730
7. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heard disease. N Engl J Med 1991;325:221-225
8. Vacek JL, Rosamond TL, Kramer PH, et al. Sex-related differences in patients undergoing direct angioplasty for acute myocardial infarction. Am Heart J 1993; 126:521-525
9. Tobin JN, Wassertheil-Smoller A, Wexler JP, et al. Sex bias in considering coronary bypass surgery. Ann Intern Med 1987;107:19-25
10. Braunwald E, Antment EM, Beasley JW, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients with Unstable Angina). J Am Coll Cardio 2000;36:970-1062
11. Azar RR, Waters DD, McKay RG, et al. Short- and medium-term outcome differences in women and men after primary percutaneous transluminal mechanical revascularization for acute myocardial infarction. Am J Cardio 2000;85:675-679
12. King KM, Ghali WA, Faris PD, et al. Sex differences in outcomes after cardiac catherization: effect modification by treatment strategy and time. JAMA 2004; 291:1220-1225
13. Tamis-Holland JE, Palazzo A, Stebbines AL, et al. Benefits of direct angioplasty for women and men with acute myocardial infarction: results of the global use of strategies to open occluded arteries in acute coronary syndromes (GUSTO II-B) Angioplasty Substudy. American Heart Journal 2004;147:133-139
14. Chandra NC, Ziegelstein RC, Rogers WJ, et al, for the National Registry of Myocardial Infarction-I. Observations of the treatment of women in the United States with myocardial infarction: A report from the National Registry of Myocardial Infarction-I. Arch Intern Med 1998;158:981-988
15. Gan SC, Beaver SK, Houck PM, et al. Treatment of acute myocardial infarction and 30-day mortality among women and men. N Engl J Med 2000;343:8-15
16. Stone PH, Thompson B, Anderson HV, et al. Influence of race, sex, and age on management of unstable angina and non-Q-wave myocardial infarction: the TIMI III Registry. J Am Med Assoc 1996;275:1104-1112
17. McCullough PA, Sandberg KR, Borzak S, et al. Benefits of aspirin and beta-blockade after myocardial infarction in patients with chronic kidney disease. Am Heart J 2002; 144:206-207
18. Berger AK, Duval S, Krumholz HM, et al. Aspirin, beta-blocker, and angiotensin-converting enzyme inhibitor therapy in patients with end-stage renal disease and an acute myocardial infarction. J Am Coll Cardio 2002;42:201-208